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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,770	02/28/2002	Dennis A. Holt	327F USC2	1514

7590 04/10/2002

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EXAMINER
COLEMAN, BRENDA LIBBY

ART UNIT	PAPER NUMBER
1624	3

DATE MAILED: 04/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/086,770	HOLT et al.
Examiner	**Art Unit**
Brenda Coleman	1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Claim 1 is are pending in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for AP1903, AP14290, AP14283, AP14291, AP14272, AP14278 and AP14279, does not reasonably provide enablement for all of the compounds embraced by the genus. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman,* 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

HOW TO MAKE: The nature of the invention in the instant case, has claims which embrace a wide range of chemically and physically distinct compounds, wherein M and Q are a substituted piperidine or pyrrolidine; and L can be a variety of functional linking groups, including heterocyclic rings. The scope of the compounds of claims 1-36 reads on a plethora of aliphatic,

heteroaliphatic, aryl and heteroaryl substituents (B^1, B^2, R^1, R^2 and R^3) and a linker moiety (L). The exact nature of these substituents are vague and indefinite in that it is not clear exactly how large the substituent may be; the position of the heteroatoms in the heteroaliphatic moiety; the size, position or point of attachment of the aryl and heteroaryl moieties; etc. While several specific multimerizing agents or monomers are disclosed, there is insufficient guidance for preparing additional multimerizing agents or monomers which would be effective in the following utilities: "e.g. to regulatably activate the transcription of a desired gene, delete a target gene, actuate apoptosis, or trigger other biological events in engineered cells growing in culture or in whole organisms, including in gene therapy applications".

There are several preferred embodiments disclosed herein. One preferred embodiment of the instant invention is multimerizing agents or monomers which have a IC50 value in the Competitive Binding FP Assay better than 1000 nM, e.g. human FKBP12. Another preferred embodiment of the compounds are those which are capable of inducing a detectable signal in a 2-hybrid transcription assay based on fusion proteins containing FKBP domain. "Preferably, the FKBP domain is an FKBP domain other than wild-type human FKBP12". Another preferred embodiment of the compounds are those which are capable of inducing a detectable signal in such an FKBP-based apoptosis assay. "Preferably, the FKBP domain is an FKBP domain other than wild-type human FKBP12".

Testing is provided for only a few of the claimed compounds at pages 13-26 of the specification. Examples should be of sufficient scope as to justify the scope of the claims.

However, the generic claims are much broader in scope than is represented by the testing. Note the broad definitions for B^1, B^2, R^1, R^2 and R^3 in the generic claims which are defined as aliphatic, heteroaliphatic, aryl or heteroaryl and L which is a linker moiety. These definitions embrace many structurally divergent groups not represented in the testing. Markush claims must be provided with support in the disclosure. Markush claims are subject to rejection based upon the lack of supporting disclosure when the "working examples" fail to include written description(s) which teach how to make and use Markush members embraced thereby in full, clear, and exact terms. See In re Fouche 169 USPQ 429. The compounds tested are not seen as adequately representative of the compounds encompassed by the extensive Markush groups instantly claimed for the uses instantly asserted and claimed.

This area of activity can be expected to be highly structure specific and unpredictable, as is generally true for chemically-based pharmacological activity. In view of the structural divergence in the claims, one skilled in the art could not reasonable extrapolate the activities of some of the claimed compounds to the other structurally divergent compounds embraced by the claims which have not been tested.

In view of the breadth of the claims, the unpredictability in this area of activity, and the limited amount of guidance and examples in the specification, one skilled in the art would have to undergo an undue amount of experimentation to prepare the claimed compounds.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reason(s) apply:

a) Claim 1 is unclear in that there are no M^1 or M^2 variables within the claim.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is (703) 305-1880. The examiner can normally be reached on Mondays and Tuesdays from 9:00 AM to 3:00 PM and from 5:30 PM to 7:30 PM and on Wednesday thru Friday from 9:00 AM to 6:00 PM.

The fax phone number for this Group is (703) 308-4734 for "unofficial" purposes and the actual number for **OFFICIAL** business is **308-4556**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brenda Coleman

Brenda Coleman
Primary Examiner AU 1624
April 8, 2002